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Claims

1. A compound of formula (I):

$$R^{1} \longrightarrow R^{2}$$

$$R^{3} \longrightarrow R^{5} \longrightarrow R^{6}$$

(I)

in which:

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 R^1 is an aryl group, optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$ alkyl, $C_{(1-6)}$ alkoxy, $C_{(1-6)}$ alkylthio, aryl $C_{(1-6)}$ alkoxy, hydroxy, halogen, CN, COR⁷, carboxy, COOR⁷, NR⁷COR⁸, CONR⁹R¹⁰, SO₂NR⁹R¹⁰, NR⁷SO₂R⁸, NR⁹R¹⁰, mono to perfluoro- $C_{(1-4)}$ alkyl, mono to perfluoro- $C_{(1-4)}$ alkoxyaryl, and aryl $C_{(1-4)}$ alkyl;

 R^2 is halogen, $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkoxy, hydroxy $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkylsulphinyl, amino $C_{(1-3)}$ alkyl, mono- or di- $C_{(1-3)}$ alkylamino $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkylcarbonylamino $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkylcarbonylamino $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkylsulphonylamino $C_{(1-3)}$ alkyl, $C_{(1-3)}$ alkylcarboxy, $C_{(1-3)}$ alkylcarboxy $C_{(1-3)}$ alkyl, and

 \mathbb{R}^3 is hydrogen, halogen, $C_{(1-3)}$ alkyl, or hydroxy $C_{(1-3)}$ alkyl; or

R² and R³ together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused 5-or 6-membered carbocyclic ring; or

 R^2 and R^3 together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused benzo or heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, $C_{(1-4)}$ alkyl, cyano, $C_{(1-3)}$ alkoxy $C_{(1-3)}$ alkyl, $C_{(1-4)}$ alkylthio, or mono to perfluoro- $C_{(1-4)}$ alkyl;

 R^4 is Het- $C_{(0-4)}$ alkyl in which Het is a 5- to 7- membered saturated heterocyclyl ring comprising N and optionally O or S, and in which N is substituted by C_{3-8} cycloalkyl or $C_{(1-6)}$ alkyl further substituted by 1, 2 or 3 substituents selected from R^{11} , $COOCH_2R^{11}$, $COOCH_2R^{11}$, COR_1^{11} , CN, $CONR_1^{12}R^{13}$, C_{3-8} cycloalkyl, vinyl optionally substituted by halogen or $C_{(1-3)}$ alkyl and a 5- to 7-membered saturated heterocyclyl ring comprising N in which N may be substituted by C_{1-3} alkyl;

 R^5 is an aryl or a heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$ alkyl, $C_{(1-6)}$ alkoxy, $C_{(1-6)}$ alkylthio, aryl $C_{(1-6)}$ alkoxy, hydroxy, halogen, CN, COR⁷, carboxy, COOR⁷, NR⁷COR⁸, CONR⁹R¹⁰, SO₂NR⁹R¹⁰, NR⁷SO₂R⁸, NR⁹R¹⁰, mono to perfluoro- $C_{(1-4)}$ alkyl and mono to perfluoro- $C_{(1-4)}$ alkoxy;

 R^6 is an aryl or a heteroaryl ring which is further optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-6)}$ alkyl, $C_{(1-6)}$ alkoxy, $C_{(1-6)}$ alkylthio, $C_{(1-6)}$ alkylsulfonyl, aryl $C_{(1-6)}$ alkoxy, hydroxy, halogen, CN, COR^7 , carboxy, COR^7 , $CONR^9R^{10}$, NR^7COR^8 , $SO_2NR^9R^{10}$, $NR^7SO_2R^8$, NR^9R^{10} , mono to perfluoro- $C_{(1-4)}$ alkyl and mono to perfluoro- $C_{(1-4)}$ alkoxy, or $C_{(5-10)}$ alkyl;

 R^7 and R^8 are independently hydrogen or $C_{(1-12)}$ alkyl, for instance $C_{(1-4)}$ alkyl (e.g. methyl or ethyl);

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 R^9 and R^{10} which may be the same or different is each selected from hydrogen, or $C_{(1-12)}$ alkyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a 5- to 7 membered ring optionally containing one or more further heteroatoms selected from oxygen, nitrogen and sulphur, and optionally substituted by one or two substituents selected from hydroxy, oxo, $C_{(1-4)}$ alkyl, $C_{(1-4)}$ alkylcarboxy, aryl, e.g. phenyl, or aralkyl, e.g benzyl, for instance morpholine or piperazine;

R¹¹ is an unsubstituted 5- or 6-membered heteroaryl or an unsubstituted 6-membered aryl, or a 5- or 6-membered heteroaryl or a 6-membered aryl substituted by one or more R¹⁴.

R¹² is selected from hydrogen or C₁₋₃alkyl;

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 R^{13} is selected from phenyl optionally substituted by halogen, C_{1-6} alkyl, C_{1-6} alkoxy or cyano, or C_{5-7} cycloalkyl;

R¹⁴ is selected from the group consisting of halogen, CF₃, C₁₋₆alkyl, C₁₋₆alkoxy or cyano; X is CH or nitrogen; and

Y is a $C_{(2-4)}$ alkylene group (optionally substituted by 1, 2 or 3 substituents selected from methyl and ethyl), CH=CH, or $(CH_2)_nS$ where n is 1, 2 or 3,

and a pharmaceutically acceptable salt thereof.

- 2. A compound according to claim 1 wherein R¹ is phenyl optionally substituted by 1, 2, 3 or 4 halogen substituents.
- 20 3. A compound according to claim 2 wherein R¹ is phenyl substituted by 1 to 3 fluoro.
 - 4. A compound according to any of claims 1 to 3 wherein X is CH and R^2 and R^3 together with the pyridone ring carbon atoms to which they are attached form a fused benzo or pyrido ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, $C_{(1-4)}$ alkyl, cyano, $C_{(1-3)}$ alkoxy $C_{(1-3)}$ alkyl, $C_{(1-4)}$ alkoxy or $C_{(1-4)}$ alkylhio, or mono to perfluoro- $C_{(1-4)}$ alkyl.
 - 5. A compound according to claim 4 wherein the fused benzo or pyrido ring is unsubstituted.
- 6. A compound according to any of claims 1 to 3 wherein X is nitrogen and R² and R³ together with the pyrimidone ring carbon atoms to which they are attached form a fused 5-membered carbocyclic (cyclopentenyl) or benzo ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, C₍₁₋₄₎alkyl, cyano, C₍₁₋₃₎alkoxyC₍₁₋₃₎alkyl, C₍₁₋₄₎alkoxy, C₍₁₋₄₎alkylthio, or mono to perfluoro-C₍₁₋₄₎alkyl.
 - 7. A compound according to claim 6 wherein the fused 5-membered carbocyclic or benzo ring is unsubstituted.
- 8. A compound according to any of claims 1 to 7 wherein R⁴ is Het C₍₀₎alkyl in which Het is a six-membered saturated heterocyclyl ring comprising nitrogen in which the nitrogen is substituted by C₃-gcycloalkyl or C₍₁₋₂₎alkyl substituted by a single substituent selected from R¹¹, COOR¹¹, COOCH₂R¹¹, COR¹¹, CN, CONR¹²R¹³, C₃₋₈cycloalkyl, vinyl optionally substituted by halogen or methyl and a 5- or 6- membered saturated heterocyclyl ring comprising N in which the nitrogen may be substituted by methyl.

(II)

- 9. A compound according to any of claims 1 to 8 wherein R^5 is phenyl and R^6 is phenyl substituted by mono to perfluoro- $C_{(1-4)}$ alkyl, halogen or $C_{(1-6)}$ alkyl.
- 5 10. A compound according to claim 9 wherein R⁶ is phenyl substituted by trifluoromethyl.
 - 11. A compound to any of claims 1 to 10 wherein Y is CH₂S.
 - 12. A compound as named in any of Examples 1 to 29.

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- 13. A pharmaceutical composition comprising a compound of formula (I) according to any of claims 1 to 12 and a pharmaceutically acceptable carrier, optionally with one or more other therapeutic compounds.
- 14. A compound of formula (I) according to any of claims 1 to 12 for use in therapy.
- 15. The use of a compound of formula (I) according to any of claims 1 to 12 for the manufacture of a medicament for treating atherosclerosis.
- 16. A method of treating a disease associated with activity of the enzyme Lp-PLA₂ which method
 20 involves treating a patient in need thereof with a therapeutically effective amount of a compound of formula (I) according to any of claims 1 to 12.
 - 17. A process for preparing a compound of formula (I) which process comprises reacting an acid compound of formula (II):

$$R^1$$
 R^2
 CO_2H

in which X, Y, R¹, R² and R³ are as hereinbefore defined, with an amine compound of formula (III):

 $R^6-R^5-CH_2NHR^4$ (III)

in which \mathbb{R}^4 , \mathbb{R}^5 and \mathbb{R}^6 are as hereinbefore defined; under amide forming conditions.